Cancer Research Center Hotline

Carotenoids and Human Health

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"Eat up your vegetables" has been a widely employed if not popular phrase for centuries, and has now been reinforced by messages from the National Institutes of Health, the American Cancer Society, the American Heart Association and other organizations concerned with disease prevention. At a recent meeting held in Honolulu, January 6-11, 2002, sponsored by the Cancer Research Center of Hawaii, about 225 delegates from 26 countries discussed their recent research which focussed on the role of carotenoid in human health. This meeting, the 13th International Carotenoid Society Symposium was organized by Dr. Bertram from the Cancer Research Center who also served as Program Chair.

Carotenoids are pigments found in leaves and in yellow and red vegetables. They play an important role in the health of both plants and animals: in plants they act to improve the efficiency of photosynthesis and to protect against photochemical damage; in animals some carotenoids are a vital source of vitamin A—for others their role in human health is just being discovered. For example, the carotenoid lutein plays a major role in plants, and research presented at this symposium suggests that it may have a similar function in the human retina. Dr. Khachik, University of Maryland, presented data showing that lutein concentrates in the macula (the yellow spot) of the human retina and is responsible for this coloration.[1] That lutein protects the retina from photodamage as it does in plants is becoming apparent from epidemiological studies linking an increased incidence of macular degeneration with low dietary intake of lutein. Dr. Bernstein, from the Moran Eye Center, University of Utah presented clinical studies demonstrating 32% lower lutein concentrations in retinas of subjects with macular degeneration vs. age-matched normal eyes. Studies were conducted in collaboration with Dr. Gellermann from the Department of Physics, University of Utah, utilizing a non-invasive spectrographic method to measure lutein levels in the human macula.[2] These clinical associations were reinforced by pre-clinical studies from another group conducted in non-human primates which demonstrated that lutein supplementation can protect against photodamage to the retina. In view of the fact that senile macular degeneration is a major cause of blindness in the elderly, affecting over 10 million Americans, the prospects for identifying high-risk individuals and for prevention of this disease seem exciting.

In Third World countries, vitamin A deficiency is a major cause of blindness in infants and of death from infectious diseases. Supplementation studies have shown that up to 50% of infant mortality can be prevented if these infants are supplied sufficient vitamin A.[3] Unfortunately, in these countries infants and young children are generally not fed diets rich in the carotenoid beta-carotene, which is broken down in the gut to yield two molecules of vitamin A. As an alternative to vitamin A supplementation—difficult in remote areas, efforts are now underway to create staple foods containing beta-carotene. This has been achieved with rice, "the golden rice project"[4] and, as was presented at this meeting by a group from Germany, has now been achieved with potatoes. In genetically engineered plants, an approximate six-fold increase in total carotenoid content in tubers was achieved. Also presented at this conference was the information that an unusual strain of banana contains beta-carotene, suggesting that the introduction of this strain in tropical communities could decrease vitamin A deficiency. While genetically modified foods are receiving a hostile reception in many regions of the world, it is difficult to understand why persuading a rice plant or a potato plant to synthesize carotenoids in its seed or tuber respectively, in addition to its leaf, could create environmental or ethical problems.

Disease prevention was also the major focus of a session devoted to the carotenoid lycopene, responsible for the red color of tomatoes, watermelon and a few other red vegetables. Epidemiological studies presented that this conference by Dr. Giovannucci, Harvard School of Public Health, have associated a 35% lower incidence of total prostate cancer and a 50% reduction of advanced prostate cancer in men consuming two to four servings of tomato sauce per week in comparison to men consuming lower amounts.[5] With this as a starting point, and the knowledge that laboratory studies in Hawaii had suggested a cancer preventive role for this carotenoid, Dr. Kucuk and colleagues at the Karmanos Cancer Center in Detroit assessed the effects of lycopene supplementation on individuals recently diagnosed with prostate cancer. A dose of 30 milligrams of lycopene/day derived from tomatoes (five to 10 times normal dietary exposure) was administered three weeks before radical prostatectomy. In comparison to controls who received no intervention, pathological examination of prostates from the lycopene-supplemented group revealed less involved margins resulting in lower Gleeson scores.[6] Interestingly, malignant tissue from supplemented individuals were found to express higher levels of connexin 43, a gene responsible for intracellular communication through gap junctions. Connexin 43 has been firmly established, in part by work by this author at the Cancer Center of Hawaii, to be a tumor suppressor gene.[7] A possible explanation for the reduction in surgical margins was presented by a group from the University of Illinois at Chicago, who showed the induction of apoptosis (programmed cell death) in lycopene treated prostate cancer cells grown in culture. These clinical studies are being pursued both in Detroit and by Dr. Clinton at the Ohio State University Comprehensive Cancer Center. If confirmed, these studies indicate an important new strategy both for prevention and treatment of prostate cancer.

Lycopene may also play a role in preventing cardiovascular disease and stroke, possibly because of its strong activity as a lipid-phase antioxidant, as suggested by recent epidemiological studies conducted by Dr. Rissanen from the University of Kupio in Finland. She presented an update on research which indicated that men in the lowest quartile of serum lycopene levels had a 3.3 fold increased risk of an acute coronary event or stroke as compared with men with higher lycopene levels. In high-risk individuals the intima-media thickness of the common carotid artery was found to be 18% greater,

as assessed by ultrasonic measurement, than in men with higher lycopene levels at lower risk of coronary event or stroke. These correlations did not hold for women who had overall higher lycopene levels indicative of a better diet.

One of the biggest disappointments in the cancer prevention community were results presented in the 1990s of a lack of protective action of beta-carotene against lung cancer and cancer in general. Epidemiological studies had strongly supported such a role for beta-carotene in smokers, yet in two intervention trials in smokers beta-carotene actually increased lung cancer rates vs. placebo controls, while in the Physicians Health Study, which contains few smokers, no protection was observed. Dr. Mayne, Yale University, presented new results on the effects of beta-carotene on the incidence of upper aero-digestive tract cancer, which predominantly appears in smokers. Interestingly, a protective effect against cancer at these sites was observed which was balanced by an increased cancer rate in the lung.[8] In all the studies showing a deleterious effect on the lung, beta-carotene was supplemented at doses approximately 10-fold higher than normally achieved in the diet. Clearly, supplementation with pharmacologic doses of beta-carotene should be avoided, especially in smokers. In an attempt to explain these findings, the research group led by Dr. Russell, at the Center on Aging at Tufts University, found that exposure of experimental animals to pharmacological doses of beta-carotene together with cigarette smoke resulted in decreased expression of a putative tumor suppressor gene in the animals' lungs together with increased cell proliferation and metaplasia. In contrast, in animals fed an amount of beta-carotene producing comparable tissue levels to those obtained in humans consuming a "healthy diet", some protection against cigarette smoke damage was observed.[9] These studies imply that at high concentrations of beta-carotene, interactions between oxygen/tobacco smoke produce lung toxins.

The carotenoids produce a colorful environment by providing pigments to leaves, flowers and fruits. They are also synthesized by microorganisms, which when consumed by animals, are responsible for the coloration of shrimp and salmon, the brilliant plumage of many birds and the yellow coloration of egg yolk. With the advent of shrimp and salmon farming, a major industry has developed to supply the carotenoid astaxanthin necessary both for the coloration of these animals and for their health. The State of Hawaii has two companies producing carotenoids from the growth of microalgae, and delegates to this conference heard details of the commercial process from representatives from Cyanotech, on the Big Island, and a Japanese company, Micro Gaia on Maui. This session was organized by Dr. Boussiba from Ben-Gurion University, Israel who presented his own experience in carotenoid production from microalgae in a desert environment.

With increasing demand for carotenoids for aquaculture, in egg production and as natural colorants for processed foods, it is apparent that the commercial importance of carotenoid production in Hawaii will increase. Moreover, it is expected that a growing realization of the importance of adequate amounts of key carotenoids in the human diet to maintain health, will also increase demand for carotenoid supplements. However, lessons learned from the beta-carotene intervention trials discussed earlier would indicate that prudent advice would be to obtain carotenoids from the diet rather than from dietary supplements. "Eat up your vegetables" has taken on new meaning.

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